UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,775	02/21/2002	Chandra S. Ramanathan	D0126 NP	5535

23914 7590 10/05/2004

STEPHEN B. DAVIS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,775	RAMANATHAN ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/12/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendix A, B & C*.

DETAILED ACTION

1. Applicant's election without traverse of Group I, drawn to nucleic acid encoding polypeptide of SED ID NO: 2, a vector and a host cell in response of 6/24/2004 is acknowledged. Applicant has elected to cancel all pending claims and replaced with it claims 22-37 drawn to the elected invention. Thus, claims 22-37 are pending and examined. Applicant has further elected nucleotide encoding SEQ ID NO: 2 and polynucleotide comprising SEQ ID NO: 1.

Specification

2. Applicant is required to update the specification by replacing the X and Y notations with appropriate SEQ ID Nos throughout the specification.

3. The title of the invention is objected to because of the use of the word "novel", which begs the novelty of issued U. S. Patents. Any invention, when patented, is novel. There is no need to say it again in the title. It is suggested that the word "novel" be deleted from the title.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4a. Claims 22-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant claims are directed to isolated polynucleotide encoding a polypeptide comprising SEQ ID No: 2 or an isolated polynucleotide comprising SEQ ID No: 1 belonging to

an alleged G protein-coupled receptor HGPRBMY25 (claims 22-27). Claims are also drawn to vectors containing the polynucleotide sequences, host cells and methods of making the polypeptide (claims 28-30). In addition, claims are also drawn to heterologous nucleic acid encoding heterologous polypeptide (claims 31-37). These claims are drawn to an invention with no apparent or disclosed patentable utility.

The applicant claims that the human HGPRBMY25 sequence encodes a 329 amino acid protein (Figure: 1, A-B) and contains structural features characteristic of G protein coupled receptor. This is presumably because of sequence homology between the instant invention (human GPCR protein sequence) and various known G protein-coupled receptors (Figure: 2). The Applicant provides relative expression levels of HGPRBMY25 in various tissue (Figures: 4 and 6). Transcripts (mRNA) corresponding to HGPRBMY25 polypeptide are expressed highly in spleen and thymus. The message is also expressed in to a significant extent in the testis and lymph node and to a lesser extent in bone marrow, spinal cord and lung. Figure 6 also shows substantial expression in female reproductive tissues such as ovary, fallopian tube and the uterus. However, there is no correlation between the message levels and the protein levels demonstrated. In addition, the instant application does not disclose the biological role of this protein or its significance. Novel biological molecules lack well-established utility and must undergo extensive experimentation.

The specification asserts that the strong homology to human G-protein coupled receptors, combined with the predominant localized expression in spleen and thymus tissue suggests the HGPRBMY25 polynucleotides and polypeptides may be useful in treating, diagnosing, prognosing, and/or preventing immune diseases and/or disorders. (page: 31,

lines7-10). Nonetheless, the specification fails to provide any sufficient information or evidence on the biological functions of the human protein encoded by the instantly claimed nucleic acid molecules, fails to show the human protein of the present invention may be effective in treatment of various disorders of the immune system, female reproductive system, as well as lung, and fails to disclose a specific, substantial asserted utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention, which does not require further research.

The specification asserts utilities of the claimed nucleic acid molecule as encoding a polypeptide of SEQ ID NO: 2 or the cDNA sequence included in the deposited clone, which is hybridizable to SEQ ID NO: 1 (page 9, lines 12-14), as having biological activity as hybridization probes for screening (page 9, lines 23-26), and screening for for the candidate compound to modulate expression levels (page 14, lines 16-22). The specification also asserts the use of the proteins encoded by the nucleic acids of the present invention in generation of antibody that binds specifically to the isolated polypeptide SEQ ID NO: 2 (page 10, lines 27-28), and identification of a binding partner to the polypeptide of SEQ ID NO: 2 (page 11, lines 12-15). However, such uses are all considered research uses only designed to identify a particular function of the claimed molecules and are not substantial utility. See, e.g., *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966) wherein a research utility was not considered a " substantial utility." Moreover, such uses are not specific to the instant molecule but applicable to any nucleic acid molecules or proteins.

The specification further asserts that the claimed nucleic acid molecules can be used to diagnose a pathological condition or a susceptibility to a pathological condition

based on the presence or absence of a mutation (page 11, 1st paragraph). The specification also asserts that based on the presence or amount of expression of the polypeptide of the instant invention in a biological sample one can diagnose a pathological condition or a susceptibility to a pathological condition (page 11, 2nd paragraph). In addition it is also asserted the instant polypeptide can also be used for preventing, treating, or ameliorating several medical conditions including immune conditions, reproductive disorders and neural disorders (pages 12, 13, and 31-33). These asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. The specification does not disclose any disease or biological disorders that are associated with the molecules of the present invention. Clearly, further research would be required to identify a disease that is associated with the molecules of the present invention. See, e.g., *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), noting, "a patent is not a hunting license. It is not a reward for the research, but compensation for its successful conclusion."

The invention also lacks a well-established utility. A well established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The sequence search of the prior art does not reveal a well-established utility for the nucleic acids. In fact, the nucleotides search of SEQ ID NO: 1 (nts 537-1523) of the present invention resulted in obtaining sequences that were 99.6% identical (see Appendix A1-3). However, these sequences have been annotated as GPCR or potential olfactory related G-coupled receptor (Accession NO: AAH31850, ABK16633 and ABK68612). In addition, amino acids sequence that is 98.8% identical to SEQ

ID NO: 2 (see Appendix B1-7) of the present invention have also been annotated as GPCR or potential olfactory G-coupled receptor (Accession NO: AAU85266, AAG71674, AAU80511, AAU95725). Furthermore, Zang et al. (2002, Accession NO; Q8VGX9) describe a mouse olfactory receptor gene, which has about 89.3% identity to SEQ ID NO: 2 of the instant invention (see Appendix C). The discrepancy between the instant disclosure, that the protein encoded by the nucleic acid molecule is immune related protein and the annotation in the art for the similar protein as being an olfactory related GPCR casts doubts on the true biological functions of the protein encoded by the nucleic acids of the present invention. Thus, the assertion that the claimed nucleic acid molecules encoding a GPCR related to immune disorders, based on the mRNA expression profile, does not endow the claimed molecules with a specific and substantial utility. No art of record discloses or suggests any property or activity for the claimed molecules such that another non-asserted utility would e well-established for the claimed invention.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 22-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5b. Further, *even if* the specification taught how to use the HGPRBMY25 polypeptide or polynucleotide encoding HGPRBMY25 of SEQ ID NO: 2, enablement would not be commensurate in scope with claims 22, 27 and 30, which are drawn to complementary nucleotide sequences to the above mentioned polynucleotide.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims reads on nucleic acid sequences which are completely complementary to nucleotide sequence that encodes a protein comprising the amino acid sequence of SEQ ID NO: 2, a nucleotide sequence of SEQ ID NO: 1. However, other than a nucleotide sequence that encodes a protein comprising the amino acid sequence of SEQ ID NO: 2, a nucleotide sequence of SEQ ID NO: 1, the specification as filed fails to disclose any other nucleotide sequences which are capable of producing the polypeptide.

Despite knowledge in the art for producing polypeptides, the specification fails to provide any guidance regarding the proteins produced by the contemplated complementary strand nucleotides and yet retain the function is lacking. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. Therefore, predicting which complementary strand generated polypeptide, if any, would retain the functions of the protein is well outside the realm of routine experimentation. Thus, an undue amount of experimentation would be required to generate the changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicants have not taught how one of skill in the art would use the full scope of polypeptide sequences encompassed by the invention of claims 22, 27 and 30. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences. Given the breadth of claims 24 and 28 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

5c. Claims 29-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* or isolated host cells does not provide enablement for a nucleotide sequence that encodes a protein comprising the amino acid sequence of SEQ ID NO: 2, a nucleotide sequence of SEQ ID NO: 1, does not reasonably provide enablement for " recombinant host cell comprising...", which encompasses the host cell, as it occurs in nature, for example, as a gene therapy patient. However, since Applicants do not intend to claim a naturally occurring products amendment of the claims to show the hand of man would obviate this rejection. It is suggested that claims 29 and 30 recite " an isolated host cell.....". Appropriate correction is required.

Deposit requirement

5d. Claims 34-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that the applicants have deposited the cDNA with ATCC (Page: 18). However, it is unclear if the deposit was made under the Budapest Treaty guidelines. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific DNA encoding protein of SEQ ID NO: 2 has been deposited under the Budapest Treaty and that the DNA will be irrevocably and without restriction or condition released to the public upon the issuance of a patent,

would satisfy the deposit requirement made herein. If the deposit is not made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable. Applicant's attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination. **The specification should be amended to include such information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information.**

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22-37 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claim 22 is rejected as being vague and indefinite because it is unclear how the applicant intends to get the complementary sequence of complementary sequence (see claim 22 (c)). Claims 23-31 are rejected insofar as they are dependent on the rejected claim 22.

6b. Claim 34 is rejected as vague and indefinite for reciting the term "HGPRBMY25" because the full meaning of an acronym should be spelled out at its first use in any claim. Claims 35-37 are rejected insofar as they are dependent on the rejected claim 34.

7. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS

September 30, 2004

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600